REMARKS

Claims 18-20, 23-26, 31-34, 37-43, 46-47, and 52 are pending in this application. Claims 18, 23, 37, 40 and 52 have been amended. Claim 53 has been cancelled.

Claims 18, 23, 37, 40 and 52 are amended to remove unnecessary limitations. Accordingly, no new matter has been added.

Applicants have not dedicated or abandoned any unclaimed subject matter, and have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Reconsideration is respectfully requested in light of the amendments and remarks below.

CLAIM REJECTIONS

The Examiner rejected 18-20, 23-26, 31-34, 37-43, 46-47, and 52 under 35 U.S.C. § 103 as allegedly obvious over Dao et al. (1997) *Blood* 89:446-56 (hereinafter "Dao") in view of Young et al. (1996) *Blood* 88:1619-31 (hereinafter "Young"). Without acquiescing to the Examiner's allegations, Applicants respectfully direct the Examiner's attention to the indicia of nonobviousness contained in the application as filed.

Applicants respectfully assert that the specification as filed provides sufficient objective evidence of the nonobviousness of claims 18-20, 23-26, 31-34, 46-47, and 52. Whenever objective evidence of nonobviousness is present, the evidence must be evaluated and the ultimate determination of patentability must be made on the entire record. *See, e.g.*, *MPEP* § 2141 (citing *In re Oetiker*, 977 F.2d 1443, 1446 (Fed. Cir. 1992)). Further, objective evidence of nonobviousness include either or both (1) the absence of an expected property or (2) a synergistic effect. *See, e.g., MPEP* § 716.02(a). As described below, the present application demonstrates BOTH the absence of an expected property and correspondingly an unexpected synergistic effect.

The Examiner alleges that Dao suggests the use of fibronectin to enhance gene transfer, and that the combination of fibronectin and flt3 ligand (FL) may ultimately replace the use of

patient-derived stromal layers. *See, e.g., Office Action dated November 3, 2005*, at p. 3. Accordingly, the Examiner's interpretation of Dao would lead an ordinarily skilled artisan to expect higher transduction efficiency of hematopoietic stem cells (HSCs) infected in the presence of fibronectin and flt3 ligand (FL) compared to HSCs infected in the presence of FL alone. However, as demonstrated by the present application, the exact opposite effect is achieved. *Specification*, at Example 9, Figure 9. Transduction of HSCs in the presence of only IL3, IL6, leukemia inhibitory factor (LIF), and FL resulted in 1.8% of transduced cells, and the addition of Retronectin™ did not increase the efficiency. *Id.*, at Figure 9. Accordingly, Applicants respectfully assert that the specification demonstrated the absence of an expected property, e.g., the absence of enhanced gene transfer into HSCs in the presence of fibronectin.

As alleged by the Examiner, Dao suggests the combination of fibronectin and FL to ultimately replace the use of stromal layers in gene transfer protocols. *See, e.g., Office Action dated November 3, 2005*, at p. 3. Further, the Examiner alleges that an ordinary artisan would have been motivated to use FL in combination with an mpl ligand and fibronectin as taught by Young since Doa teaches that FL might be essential to viability absent stromal support. *Id.* Accordingly, an ordinarily skilled artisan would expect fibronectin to replace, or be redundant with, the beneficial effects of stromal support on transduction, particularly in light of the fact that it does not enhance transduction of HSCs cultured with stromal support and in the presence of other cytokines including LF. *See, .e.g., Specification*, at Example 9, Figure 9. In other words, an ordinarily skilled artisan would not expect fibronectin to synergize with thrombopoietin (TPO) to enhance gene transfer. However, the present application provides evidence that fibronectin unexpectedly synergizes with thrombopoietin to significantly increase transduction of HSCs. The present application demonstrates that although fibronectin alone had no effect on enhancing transduction of HSCs cultured with IL3, IL6, LF, and FL, and although TPO alone enhanced transduction of HSCs cultured with IL3, IL6, LF, and FL by about two-fold, the combination of both fibronectin and TPO enhanced transduction of HSCs cultured with IL3, IL6, LF, and FL by about four-fold. *Id.* Accordingly, fibronectin and TPO have a more than additive effect, i.e., a synergistic effect, on the transduction of HSCs.

In light of the above evidence of nonobviousness, i.e., the demonstration of the absence of an expected property and the demonstration of unexpected synergistic effects, Applicants respectfully submit that the present claims are not obvious. As such, Applicants request immediate allowance of claims18-20, 23-26, 31-34, 46-47, and 52.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance and early notification to that effect is respectfully requested. Applicants respectfully reserve the right to appeal should the Examiner continue to disagree as to the patentability of the presently-claimed invention. If the Examiner believes there are further unresolved issues that could be resolved by discussion, the Examiner is respectfully requested to phone the undersigned at (415) 318-1212.

The Commissioner is hereby authorized to charge any fees associated with this communication, including any necessary fees for additional claims, and/or credit any overpayment to Deposit Account No. 504616 (Our Ref. No. 46583-105151).

Respectfully submitted,
KING & SPALDING, LLP

Dated: 11/3/08

By: _____
Todd A. Lorenz, Reg. No. 39,754

Customer Number: 80964

KING & SPALDING LLP
Four Embarcadero Center, Suite 3500
San Francisco, California 94104-1513
Telephone: (415) 318-1200
Facsimile: (415) 318-1300